DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

P940008

Memorandum

Date NOV 28 1995

From Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of Intermedics, Inc.
Res-Q™ ACD (Arrhythmia Control Device) Epicardial Patch and Non-thoracotomy Lead (NTL) Systems - ACTION

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

for Susan Alpert, Ph.D., M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved _____ Disapproved _____ Date _____

DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

[DOCKET NO. _____]

Intermedics, Inc.; PREMARKET APPROVAL OF Res-Q™ ACD (Arrhythmia Control Device) Epicardial Patch and Non-thoracotomy Lead (NTL) Systems

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by Intermedics, Inc., Angleton, Texas, for premarket approval, under section 515 of the Federal Food, Drug, and Cosmetic Act (the act), of Res-Q™ ACD (Arrhythmia Control Device) Epicardial Patch and Non-thoracotomy Lead (NTL) Systems. After reviewing the recommendation of the Circulatory System Devices Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter on November 28, 1995, of the approval of the application.

FOR FURTHER INFORMATION CONTACT:

Carole C. Carey

Center for Devices and Radiological Health (HFZ-450)

Food and Drug Administration

9200 Corporate Boulevard

Rockville, MD 20850

301-443-8609.

SUPPLEMENTARY INFORMATION: On March 17, 1994, Intermedics, Inc., Angleton, Texas 77515, submitted to CDRH an application for premarket approval of Res-Q™ ACD (Arrythmia Control Device) Epicardial Patch and Non-thoracotomy Lead (NTL) Systems which consists of the following: model 101-01 & 101-01R Res-Q™ implantable arrhythmia control device; model 531-30 Rx2OOO GRAPHICS program module to be used with Intermedics commercially available model 522-06 Rx2OOO GRAPHICS programmer; models 497-05, 497-06, and 497-09 right ventricular (RV) defibrillation/pacing leads; model 497-15 subcutaneous patch lead; model 49716 superior vena cava (SVC) leads; models 497-01, 497-02, 497-11, and 497-12 epicardial patch leads; models A67 and L67 commercially available CPI® epicardial patch leads; model 370-01 adapter; model 370-21 Y-adapter; model 370-04 Test Box; models

370-03 and 370-23 Patient Cables; model 370-05 Test Load; model 370-02 Accessory Kit; model 370-10 Lead Caps; and models 370-11, 370-12, 370-13, 370-14, 370-15, 370-16, 370-48, and 370-49 Stylets. The device is a automatic, implantable cardioverter-defibrillator system (ICD) and is indicated for use in patients who are at high risk of sudden death due to ventricular arrhythmias and have experienced one of the following situations: (1) survival of at least one episode of cardiac arrest (manifested by a loss of consciousness) due to a ventricular tachyrhythmia, or (2) recurrent, poorly tolerated sustained ventricular tachycardia (VT). Note: The clinical outcome for hemodynamically stable, sustained-VT patients is not fully known. Safety and effectiveness studies have not been conducted.

On November 28, 1995, CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

OPPORTUNITY FOR ADMINISTRATIVE REVIEW

Section 515(d)(3) of the act (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act (21 U.S.C. 360e(g)), for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under part 12 (21 CFR part 12) of FDA's administrative practices and regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 10.33(b) (21 CFR 10.33(b)). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h), (21 U.S.C. 360e(d), 360j(h)) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated:_____.

_____

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

NOV 28 1995

Ms. Kathleen M. Chester
Regulatory Affairs Specialist
Intermedics, Inc.
4000 Technology Drive
Angleton, Texas 77515

Re: P940008
Res-Q™ ACD (Arrhythmia Control Device) Epicardial Patch and Non-thoracotomy Lead (NTL) Systems
Dated: March 17, 1994
Received: December 9, 1994, and January 11, February 15, April 24, April 27, May 30, June 9, July 31, August 3, August 21, September 12, and November 13, 1995

Dear Ms. Chester:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Res-Q™ ACD (Arrythmia Control Device) Epicardial Patch and Non-thoracotomy Lead (NTL) Systems which consist of the following: model 101-01 & 101-01R Res-Q™ implantable arrhythmia control device; model 531-30 Rx2000 GRAPHICS program module to be used with Intermedics commercially available model 522-06 Rx2000 GRAPHICS programmer; models 497-05, 497-06, and 497-09 right ventricular (RV) defibrillation/pacing leads; model 497-15 subcutaneous patch lead; model 497-16 superior vena cava (SVC) leads; models 497-01, 497-02, 497-11, and 497-12 epicardial patch leads; models A67 and L67 commercially available CPI® epicardial patch leads; model 370-01 adapter; model 370-21 Y-adapter; model 370-04 Test Box; models 370-03 and 370-23 Patient Cables; model 370-05 Test Load; model 370-02 Accessory Kit; model 370-10 Lead Caps; and models 370-11, 370-12, 370-13, 370-14, 370-15, 370-16, 370-48, and 370-49 Stylets. This device is indicated for use in patients who are at high risk of sudden death due to ventricular arrhythmias and have experienced one of the following situations: (1) survival of at least one episode of cardiac arrest (manifested by a loss of consciousness) due to a ventricular tachyarrhythmia, or (2) recurrent, poorly tolerated sustained ventricular tachycardia (VT). Note: The clinical outcome for hemodynamically stable, sustained-VT patients is not fully known. Safety and effectiveness studies for this indication have not been conducted. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions

of Approval for Implantable Defibrillators and Programmers" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

Expiration dating for this device has been established and approved at eleven months shelf life. The storage temperature is between -5°C (23°F) to 55°C (131°F).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that as soon as possible, and before commercial distribution of your device, that you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form, including the patient manual. In addition, on November 22, 1995, you committed to providing a PMA supplement with a revised patient manual which more appropriately addresses the needs of the patient.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

In addition, under section 522(a) of the act, manufacturers of certain types of devices identified by the act or designated by FDA are required to conduct postmarket surveillance studies. FDA has identified under section 522(a)(1)(A) the above noted device as requiring postmarket surveillance.

Upon approval and within thirty (30) days of first introduction or delivery for introduction of this device into interstate commerce you will be required to submit to FDA certification of the date of introduction into interstate commerce, a detailed protocol which describes the postmarket surveillance study, and a detailed profile of the study's principal investigator that clearly establishes the qualifications and experience of the individual to conduct the proposed study. For your information, general guidance on preparing a protocol for a postmarket surveillance study is enclosed.

At that time you should submit five (5) copies to:

Postmarket Studies Document Center
1350 Piccard Drive (HFZ-544)
Rockville, Maryland 20850

Within sixty (60) days of receipt of your protocol, FDA will either approve or disapprove it and notify you of the Agency's action in writing. Do not undertake a postmarket surveillance study without an FDA approved protocol.

Failure to certify accurately the date of initial introduction of your device into interstate commerce, to submit timely an acceptable protocol, or to undertake and complete an FDA approved postmarket surveillance study consistent with the protocol, will be considered violations of section 522.

In accordance with the Medical Device Amendments of 1992, failure of a manufacturer to meet its obligations under section 522 is a prohibited act under section 301(q)(1)(C) of the act (21 U.S.C. 331(q)(1)(C)). Further, under section 502(t)(3) of the act (21 U.S.C. 352(t)(3), a device is misbranded if there is a failure or refusal to comply with any requirement under section 522 of the act. Violations of sections 301 or 502 may lead to regulatory actions including seizure of your product, injunction, prosecution, or civil money penalties or other FDA enforcement actions including (but not limited to) withdrawal of your PMA.

If you have any questions concerning postmarket surveillance study requirements, contact the Postmarket Surveillance Studies Branch, at (301) 594-0639.

Under section 519(e) of the act (as amended by the Safe Medical Devices Act in 1990), manufacturers of certain devices must track their products to the final user or patient so that devices can be located quickly if serious problems are occurring with the products. The tracking requirements apply to (1) permanent implants the failure of which would be reasonably likely to have serious adverse health consequences; (2) life sustaining or life supporting devices that are used outside of device user facilities the failure of which would be reasonably likely to have serious adverse health consequences; and (3) other devices that FDA has designated as requiring tracking. Under section 519(e), FDA believes that your device is a device that is subject to tracking because it is a permanent implant whose failure would be reasonably likely to have serious adverse consequences.

FDA's tracking regulations, published in the FEDERAL REGISTER on August 16, 1993, appear at 21 CFR Part 821. These regulations set out what you must do to track a device. In addition, the regulations list example permanent implant and life sustaining or life supporting devices that FDA believes must be tracked at 21 CFR § 821.20(b) and the devices that FDA has designated for tracking at 21 CFR § 821.20(c). FDA's rationale for identifying these devices is set out in the FEDERAL REGISTER (57 FR 10705-10709 (March 27, 1991), 57 FR 22973-22975 (May 29, 1992), and 58 FR 43451-43455 (August 16, 1993)).

If you have questions concerning this approval order, please contact Carole Carey at (301) 443-8609.

Sincerely yours,

Philip J. Phillips

for Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosures

Summary of Safety and Effectiveness Data

P940008

✦✦✦

Intermedics, Inc.

Res-Q™ ACD Epicardial Patch and Non-thoracotomy Lead Systems

✦✦✦

Date of Panel Recommendation
August 21, 1995

Date of Notice of Approval
November 28, 1995

Food and Drug Administration
Center for Devices and Radiological Health
Office of Device Evaluation
Division of Cardiovascular Respiratory and Neurological Devices

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SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name:	Automatic Implantable Cardioverter Defibrillator System
Device Trade Name:	Res-Q™ ACD Model 101-01 & 101-01R Epicardial Patch and Non-thoracotomy Lead (NTL) Systems
Applicant's Name/Address:	Intermedics Inc. 4000 Technology Drive Angleton, Texas 77515
PMA Number:	P940008
Date of Panel Recommendation:	August 21, 1995
Date of Notice of Approval to Applicant:	November 28, 1995

II. INDICATIONS FOR USE

The Res-Q™ ACD is indicated for use in patients who are at high risk of sudden death due to ventricular arrhythmias and have experienced one of the following situations: (1) survival of at least one episode of cardiac arrest (manifested by a loss of consciousness) due to a ventricular tachyarrhythmia, or (2) recurrent, poorly tolerated sustained ventricular tachycardia (VT). NOTE: The clinical outcome for hemodynamically stable, sustained-VT patients is not fully known. Safety and effectiveness studies for this indication have not been conducted.

III. DEVICE DESCRIPTION

The Res-Q™ ACD System consists of the following: model 101-01 & 101-01R Res-Q implantable arrhythmia control device; model 531-30 Rx2000™ GRAPHICS program module to be used with Intermedics commercially available model 522-06 Rx2000™ GRAPHICS programmer; models 497-05, 497-06, and 497-09 right ventricular (RV) defibrillation/pacing leads; model 497-15 subcutaneous patch lead; model 497-16 superior vena cava (SVC) lead; models 497-01, 497-02, 497-11, and 497-12 epicardial patch leads; models A67 and L67 commercially available CPI® epicardial patch leads; model 370-01 adapter; model 370-21 Y-adapter; model 370-04 Test Box; models 370-03 and 370-23 Patient Cables; model 370-05 Test Load; model 370-02 Accessory Kit; model 370-10 Lead Caps; and models 370-11, 370-12, 370-13, 370-14, 370-15, 370-16, 370-48, and 370-49 Stylets.

A. The Res-Q™ ACD

The Res-Q™ ACD is a multiprogrammable, implantable arrhythmia control device with antitachycardia pacing/cardioversion/defibrillation and single-chamber bradycardia pacing capabilities (in ventricular demand inhibited or VVI mode). The Res-Q™ ACD circuitry is housed in a hermetically sealed titanium case and consists of discrete electrical components, hybrid circuit assemblies, batteries, high-voltage capacitors, a crystal, and a telemetry coil. The header is made of epoxy and provides for electrical

connection to the pacing and defibrillation leads. The header on the model 101-01 accepts two 4-mm defibrillation connectors (Intermedics' standard defibrillation lead connector size) and one VS-1 (an intra-industry standard for lead-to-pulse generator connection) pace/sense connector. The header on the model 101-01R accepts two 6.1-mm defibrillation connectors and one pace/sense connector between 4.75 to 5-mm. The Res-Q™ ACD weighs approximately 240 grams with a volume of about 150 cc (160 cc for the model 101-01R).

1. Arrhythmia Detection

A sensed rate, with a programmable range of 90 - 300 bpm is used by the Res-Q™ ACD as the primary detection criterion. By programming the rate boundaries into distinct areas, this allows the classification of all possible rates into three broad regions: a sinus rate (which is the patient's intrinsic rhythm), tachycardia, and fibrillation regions. The tachycardia region can be further subdivided into as many as three zones. In addition to high rate, there are four detection criteria (used alone or combined) to classify heart rhythms as arrhythmias: high rate, sudden onset, rate stability, and sustained high rate. These four enhancements are combined to form ten different programmable tachycardia detection algorithms (independently programmable for each tachycardia zone). When tachycardia detection is met, the device will initiate its programmed treatment. A redetection criteria which use high rate and rate stability algorithms are used to determine whether tachycardia was terminated. The fibrillation detection is satisfied when a preselected number of high rate intervals (four to 30 in increments of one) fall within the defined fibrillation (FIB) region (175 to 300 bpm) or when a programmable number of FIB intervals, *x* (five to 31 in increments of one) out of a programmable number of total intervals, *y* (five to 31 in increments of one) falls into the fibrillation region. The detection of sinus rhythm post-shock or antitachycardia therapy also uses an '*x* out of *y*' algorithm. In the bradycardia pacing mode, the Res-Q™ ACD operates in the ventricular demand inhibited (VVI) mode. Signals occurring at rates faster than 39 events per second are sensed as electrical interference ("noise"). The device will initiate either asynchronous (VOO) pacing at the programmed rate or nonpacing (OOO) operation, depending on the programmed noise reversion mode. The sensing system uses automatic gain control (AGC) with a maximum sensitivity of 0.15 mV which can be programmed ON or OFF.

2. Therapy

The Res-Q™ ACD can deliver four antiarrhythmic therapies: "A" (adaptive autodecremental burst), "B" (adaptive scanned burst), "C" (low-energy shock), and "D" (high energy shock). The number of programmable therapies is any combination of A, B, C, or D for each tachycardia and fibrillation zone. If both pacing and shock therapies (A, B or C) are programmed in a given tachycardia zone, pacing therapies will be delivered before the delivery of a shock. However, therapy D is restricted to shock therapy only and only shock therapies can be programmed in the fibrillation zone. The basic therapeutic modality for antitachycardia pacing is a burst of one or more pacing stimuli. Therapeutic shocks can be delivered between 50 (about 0.2 joules) to 700 volts (about 40 joules). The actual energy delivered is dependent on the impedance of the shock electrode system. The shock waveform is biphasic with a fixed pulse width of 10 msec (6.5 msec for the first phase and 3.5 msec for the second phase).

3. Diagnostics

The Res-Q™ ACD provides the following diagnostic capabilities: (1) non-invasive programmed stimulation (NIPS) used for arrhythmia induction and/or electrophysiologic studies; (2) programmer display of surface ECG and intracardiac electrogram; (3) diagnostic event counters including: cardiac cycle data, arrhythmia therapy history, total shocks, and details of last shock; (4) battery status indication via the Battery Charge-Time Test, Battery/Capture Test and/or the postcharge battery voltage; (5)

verification of proper capture via the Battery/Capture Test; (6) verification of proper sensing via the Intrinsic Rhythm Sensing Test and Maximum Sensitivity Test; and (7) shock impedance measurement via the Shock Electrode Integrity Test.

B. Model 531-30 Rx2000™ Graphics Program Module

The model 531-30 Rx2000™ GRAPHICS program module is an electronic memory cartridge which contains the instructions to program and obtain data from the Intermedics Res-Q™ ACD. With the use of a Rx2000™ GRAPHICS Programmer, the model 531-30 enables the user to interrogate and program the Res-Q™ ACD as well as perform other programmer functions. The program module consists of a printed circuit board containing memory integrated circuits encased in a protective plastic housing that inserts into a receptacle on the front of the programmer.

C. Model 370-04 Test Box with Model 370-03 or Model 370-23 Patient Cables

The model 370-04 Test Box is a battery powered device designed to facilitate implant testing of the Res-Q™ ACD by providing switch selectable connections between the patient, the packaged Res-Q™ ACD, ECG, and standard auxiliary equipment. It also provides a means of rapid electrical disconnection to protect the patient, the Res-Q™ ACD, and auxiliary equipment from potential damage by external defibrillation. The test box consists of a plastic box housing, a patient cable connector, a cable which provides direct connection to the Res-Q™ ACD package, a function selection switch and two sets of binding posts for external ECG and auxiliary equipment connections. The models 370-03 and 370-23 Patient Interface Cables enable complete testing of the Res-Q™ ACD system during an implant by providing direct connection between implanted leads and either the model 370-04 Test Box or the Res-Q™ ACD package. The patient cables are approximately twelve feet in length and are encased in a silicone rubber jacket.

D. Lead Systems

The Res-Q™ Patch System consists of either a model 101-01 Res-Q™ ACD used in combination with any two of four Intermedics' Epicardial Patches (a model 497-01 small oval, model 497-02 large oval, model 497-11 right ventricular conformal patch, and model 497-12 left ventricular conformal patch) or a model 101-01R used in conjunction with two CPI® Patches: model A67 (also known as model 0040 small patch) or model L67 (also known as model 0041 large patch). Model 370-01 step down adapters allow use of the CPI® Patches with the model 101-01 Res-Q™ ACD.

The Res-Q™ NTL system consists of three possible lead configurations used in conjunction with the model 101-01 Res-Q™ ACD: (1) a right ventricular (RV) lead (model 497-05, model 497-06, or model 497-09 lead) used in combination with a subcutaneous patch (model 497-15), (2) a RV lead used in combination with a Superior Vena Cava (SVC) lead (model 497-16), or (3) a RV lead used in combination with both a subcutaneous patch and an SVC lead adapted together by a model 370-21 Y-adapter.

IV. CONTRAINDICATIONS

The use of the Res-Q™ ACD is contraindicated in patients with ventricular tachyarrhythmias due to transient conditions, including: myocardial ischemia, acute myocardial infarction, drug toxicity, arrhythmogenic drug response, electrolyte imbalances, hypoxia or other causes of transient arrhythmias (e.g., electrocution).

V. WARNINGS

Handling

- The Res-Q™ ACD has been deactivated before shipping. When an Inquire operation is performed with the Rx2OOO GRAPHICS Programmer, a message should appear, as follows: ATTENTION! THE DEVICE HAS BEEN DISABLED FOR HANDLING OR TESTING. ALL AUTOMATIC DEFIBRILLATION AND ANTITACHYCARDIA RESPONSES ARE DISABLED.
- The Res-Q™ ACD should be disabled before: handling, disconnection of the package connector assembly, or lead connection. If an appropriate message does not appear when the device is inquired, select IMPLANT AND FOLLOW-UP SUPPORT on the Res-Q™ Functions menu to access a screen allowing the device to be disabled for handling.
- Do not incinerate the Res-Q™ ACD.

External Defibrillation

- Use of an external defibrillator may damage the Res-Q™ ACD.
- Do not attach an external defibrillator to the Res-Q™ ACD Test Box, as any shocks would be delivered through the defibrillation coil or patch electrodes and could cause severe tissue damage.
- The function selector switch of the model 370-04 Res-Q™ ACD Test Box must always be turned to SAFE before defibrillating with either internal or transthoracic paddles from an external (conventional) defibrillator. If the model 370-04 Test Box is not being used, all equipment should be disconnected from the patient before defibrillating with either internal or transthoracic paddles from any external defibrillator.

Lead Compatibility

- Use only functionally compatible patch and nonthoracotomy leads with the Res-Q™ ACD. Intermedics and CPI epicardial patches as well as Intermedics non-thoracotomy leads were used within the clinical protocol (*see the list of compatible lead models in device description on page 1*).

Implantation

- The physician should read the product literature for all components of the Res-Q™ ACD system prior to implantation. Technical support should be requested from Intermedics Clinical Engineering.
- **Do not perform the Self-Test after the Res-Q™ ACD has been connected to the patient, as it generates a full-energy shock.**
- A shock electrode impedance of 20 ohms or less (when measured following a shock ≥ 200 V) can damage the Res-Q™ ACD.
- Electromagnetic interference (noise) can cause the Res-Q™ ACD to inappropriately deliver shocks. Intracardiac electrograms should be monitored for the presence of signals of noncardiac origin. If events other than intrinsic rhythms are sensed, reposition the patient interface cable or the Res-Q™ ACD Test Box or ground the patient.
- Avoid extremely long fibrillation bursts during the Defibrillation Threshold Test, as the bursts cannot be prematurely terminated.
- Complete interaction testing must be performed before the Res-Q™ ACD is implanted in a patient with a pacemaker.

Programming

- The Res-Q™ ACD may not reliably differentiate between SVT (supra ventricular tachycardia) and VT if A-V conduction is intact. Patients with SVT should be carefully evaluated so that the Res-Q™ ACD's tachycardia detection algorithm will not interpret SVT as a ventricular arrhythmia.
- Use of a tachycardia response mode should be considered only after evaluation of appropriate EP (electrophysiology) data, including all aspects of the episodes and serial drug testing. Assessment of the patient's cardiac rate in response to exercise is especially important in determining the optimal tachycardia recognition algorithm.

Follow-up

- The magnet must be held in place to continue inhibition of antitachyarrhythmia detection and responses.

Sterilization

- Do not resterilize the device. If sterility is compromised, return the entire contents to Intermedics.

Explantation

- A device explanted for any reason must not be reused for implantation in another patient.
- Deactivate the Res-Q™ ACD prior to explantation to minimize the possibility of inadvertent shock delivery. All explanted components should be returned to Intermedics.

Operational

- No antiarrhythmic therapies will be delivered when the Res-Q™ ACD is in the backup mode.
- There is no bradycardia pacing when the device is charging to deliver therapy.

Magnetic Resonance Imaging (MRI)

- Do not expose patients with implanted defibrillators to MRI equipment.

VI. PRECAUTIONS

Implantation

- The Res-Q™ ACD should only be implanted abdominally.

Storage

- Do not expose the Res-Q™ ACD to temperatures below -5°C (23°F) or above 55°C (131°F). Exposures to temperatures outside this range may adversely affect the operation of the device.

Effects of Drugs

- While the use of some cardiac drugs, such as amiodarone, may affect pacing and/or defibrillation thresholds, no drug therapy has been reported as contraindicated in the management of a pacing device recipient. However, alteration of a patient's pharmacologic regimen may affect the device's ability to terminate tachycardia or fibrillation, or may alter the rate of tachycardia or fibrillation and hence, the device's response.

Programming

- **Programming a large number of intervals for the sustained-high-rate criterion may delay the tachycardia response for up to 204 minutes** if the primary tachycardia detection criteria are not met. Prior to programming the sustained-high-rate criterion, patients should be evaluated for tolerance of their

tachycardia for extended time periods, and those patients who experience hemodynamic compromise should not use sustained high rate or should be programmed to a small number of sustained-high-rate intervals.

- Noninvasive programmed stimulation should be performed only when proper emergency facilities for cardioversion and defibrillation are available. An adequate number of experienced personnel must be present during the procedure.
- Asynchronous pacing into sinus rhythm can induce an arrhythmia.
- Programming a fixed sensitivity may result in non-detection of arrhythmias.
- The Res-Q™ ACD should only be programmed with the Rx2000™ GRAPHICS Programmers with Part Number 0160323101 or above. The part number appears on a small white label affixed to the lip of the case, directly beneath the cooling fan on the back of the unit.
- During any inquire or programming operation, you may observe device inhibition or reversion to the noise rate for a few pacing or sensing cycles.
- Any programming operations, e.g., change of detection or response parameters or simply pressing the PROGRAM DISPLAY key, carried out while a tachycardia is under way will cause the device to recommence the detection process. Note that if sudden onset is one of the required criteria when programming is done during a tachycardia, the algorithm will not be satisfied (since sudden onset cannot be assessed in the midst of a tachycardia). Thus, no response can take place.
- The power levels required to generate many pulses in a short period result in a temporary decline in the output voltage delivered by the device during a burst. This phenomenon, referred to as voltage droop, is a function of pulse width, pulse amplitude and burst rate, and is magnified by low lead impedance.
- Interruption of the programming sequence or loss of communication between the device and the programmer may result in incomplete data transmission. A message will appear that informs the physician of this condition.

Environmental Hazards

Source	Possible Effects	Recommendations
Cellular Phones (e.g., portable and mobile cellular phones)	- Unpredictable defibrillator response, including reversion to asynchronous pacing or the OOO mode, complete inhibition or generation of antitachycardia/cardioversion/ defibrillation responses (Potential effects may be due to either the radio frequency signal or the magnet within the phone)	- To restore the defibrillator's operational state, move the phone away from the device - Maintain a minimum separation of 15 cm (6 in) between the phone's antenna and defibrillator; for phones transmitting above three watts, maintain a minimum separation of 30 cm (12 in) - If the phone is in the listen or standby mode, do not carry it in a breast pocket or on a belt within the above-stated range

Source	Possible Effects	Recommendations
Electrocautery	- Unpredictable defibrillator response, including reversion to asynchronous pacing or the OOO mode, complete inhibition or generation of antitachycardia/cardioversion/ defibrillation responses and damage to defibrillator circuitry or cardiac tissue - Reversion to elective replacement parameters - Reversion to backup mode - Permanent damage to system (if sufficient energy applied) - Burn muscle tissue adjacent to lead electrodes - Cardiac arrhythmias	- Deactivate defibrillator - Apply in short bursts with ground plate positioned to minimize current flow to pacing system - Continuously monitor patient's peripheral pulse during treatment - Check defibrillator for proper operation immediately following procedure - Follow the backup-reset procedure, if necessary
External Defibrillation	- The use of an external defibrillator may damage the Res-Q™ ACD - Damage to cardiac tissue adjacent to stimulating electrodes or tissue surrounding the implanted defibrillator, leading to possible alteration in thresholds - Reversion to elective replacement parameters - Unpredictable defibrillator response may include reversion to asynchronous pacing or the OOO mode, complete inhibition or generation of antitachycardia/cardioversion/ defibrillation responses and damage to defibrillator circuitry or cardiac tissue - Reversion to backup mode	- Place paddles as far from implanted defibrillator as possible - Avoid putting implanted defibrillator in direct path of current flow - Monitor implanted defibrillator performance during and after treatment - Reposition (or replace) leads - Reprogram or replace implanted defibrillator - Follow the backup-reset procedure, if necessary

Source	Possible Effects	Recommendations
Home Appliances (e.g., defective microwave ovens, electric razors, electric power tools and electrical ignition systems [including those used on gasoline-powered devices])	- Unpredictable defibrillator response, including reversion to asynchronous pacing or the OOO mode, complete inhibition or generation of antitachycardia/cardioversion/ defibrillation	Where appropriate, provide specific warning or reprogram defibrillator to minimize susceptibility
Lithotripsy	- No established data exists	- Equipment and sufficient competent staff to handle emergencies should be available and patient's pulse should be monitored continuously during the procedure - Check defibrillator for proper operation immediately following procedure
Medical Diathermy (Short-wave Thermal Induction)	- Unpredictable defibrillator response, including reversion to asynchronous pacing or the OOO mode, complete inhibition or generation of antitachycardia/cardioversion/ defibrillation responses and damage to defibrillator circuitry or cardiac tissue	- Do not expose patients to this type of equipment - If necessary, apply away from the immediate vicinity of defibrillator and lead system - Deactivate defibrillator - Continuously monitor patient's peripheral pulse during treatment - Check defibrillator for proper operation immediately following procedure

Source	Possible Effects	Recommendations
Nuclear Magnetic Resonance / Magnetic Resonance Imaging	- Complete inhibition of output - Permanent effect on system cannot be ruled out	- **Do not expose patients with implanted defibrillators to MRI equipment** - Disable all antiarrhythmic functions - Use as external defibrillator and provide sufficient competent staff to handle emergencies if NMR/MRI is unavoidable - Continuously monitor patient's peripheral pulse during treatment - Check defibrillator for proper operation immediately following procedure
Other Sources of Electromagnetic Interference (EMI) (e.g., electronic article surveillance [store security] systems, environments with operating electric arc welders, electric smelting furnaces, radio and television transmitters [amateur "ham" and CB radios], high-power radar transmitters, and power-generating facilities)	- Environments capable of producing intense electromagnetic fields can interfere with proper pacing, causing inappropriate antitachycardia bursts or shocks, noise reversion, inhibition of device output - Reversion to backup mode	- Consider intensities of the electromagnetic fields encountered by the patient - Where appropriate, provide specific warnings or reprogram defibrillator to minimize susceptibility - Adjust patient's occupation/lifestyle to reduce exposure to EMI sources that are likely to cause interference - Disable all antiarrhythmic functions

Source	Possible Effects	Recommendations
Therapeutic Radiation (e.g., linear accelerators and cobalt machines used in cancer treatment)	- Ranges from temporary disturbance of device function to permanent damage	- Protect defibrillator with local radiation shielding - Relocate defibrillator if tissue near implant site must be irradiated with high, cumulative dosages - Monitor defibrillator's performance during and after treatment

VII. ADVERSE EVENTS

The Res-Q™ ACD clinical investigations involved 466 devices implanted in 413 patients and 8,272 cumulative implant months (mean implant duration was 20 months). The 130 observations and 70 complications presented in the tables below reflect the relevant clinical experience with the Res-Q™ ACD (events which were related to early design/manufacturing problems and now resolved are not presented). See Tables 1 and 2. None of the 58 patient deaths reported during the clinical investigation were attributed to the Res-Q™ ACD. Rates of occurrence of observations and complications reported in the Res-Q™ ACD study were the same rates of adverse events experienced by other manufacturers with similar products.

A. Clinical Observations

Table 1. Summary of Clinical Observations
All patients treated: Patch (N =178 Patients) & NTL(N=235 Patients) (Total Device Months = 8272)

Observations	Results	Number Events (E) (N=130)	Incidence Rate (%E/ Device Months)	Mean Time Between Events (Months)
Oversensing		(26)	0.31	318
T-waves (7)	Shock delivery	14		
Myopotentials (6)	No effect	9		
Unknown (6)	Prolonged pacing intervals	2		
P-waves (3)	Sinus rhythm not detected	1		
R-waves (3)				
Post-shock (1)				
Inappropriate detection/therapy programming		(22)	0.27	376
	Shock delivery during exercise	9		
	No therapy delivered	4		
	Shock delivery	4		
	Prolonged therapy delivery	3		
	Shock delivery due to VT acceleration	1		
	Shock delivery due to VT acceleration from ATP	1		

Observations	Results	Number Events (E) (N=130)	Incidence Rate (%E/ Device Months)	Mean Time Between Events (Months)
Unidentified etiology		(22)	0.27	376
	Shock delivery	8		
	Inaccurate diagnostics/ erroneous data	5		
	Backup mode	4		
	Autogain disabled	3		
	Device disabled	1		
	Parameter error	1		
Electrocautery		(12)	0.15	689
	Backup mode	6		
	Shock delivery	6		
Patient/device interaction		(11)	0.13	752
	Device discomfort	2		
	Shock delivery due to incessant VT	2		
	Communication difficulty	1		
	Defibrillation impedance change	1		
	Epicardial patch migration	1		
	Inconsistent R-wave measurement at implant	1		
	Inadequate lead length	1		
	Lead dislodgement	1		
	Oversensing due to low R-wave amplitudes	1		
SVT	Shock delivery	(9)	0.11	919
Communication errors		(7)	0.08	1182
	Noise-induced programmer interaction	3		
	Autogain disabled	1		
	No therapy delivered	1		
	Parameter error	1		
	Telemetry/INQUIRE interaction	1		
High pacing thresholds		(6)	0.07	1379
	Intermittent capture	3		
	Loss of capture	3		
Undersensing		(6)	0.07	1379
	Inappropriate pacing	5		
	Inappropriate post-shock pacing	1		

Observations	Results	Number Events (E) (N=130)	Incidence Rate (%E/ Device Months)	Mean Time Between Events (Months)
User error		(6)	0.07	1379
	Incorrect ROM module version	2		
	Autogain disabled	1		
	Delayed therapy delivery	1		
	Inaccurate diagnostics	1		
	Inadvertent use of USER PRESETS	1		
High pacing output	Diaphragmatic stimulation	(2)	0.02	4136
Excessive manual Shocks	Premature ERI indicator	(1)	0.01	8272

B. Clinical Complications

Table 2. Summary of Clinical Complications
All patients treated: Patch (N =178 Patients) & NTL(N=235 Patients) (Total Device Months = 8272)

Complications	Results	Number Events (E) (N=130)	Incidence Rate (%E/ Device Months)	Mean Time Between Events (Months)
Patient/device interactions		(18)	0.22	460
	Infection	12		
	Hematoma at subcutaneous patch site	1		
	Loss of capture (cardiac sarcoidosis)	1		
	Loss of communication (pocket problem)	1		
	Pocket necrosis	1		
	Shock delivery (SVT)	1		
	Thrombosis	1		
Lead dislodgement		(10)	0.12	827
	Shock delivery	4		
	Loss of capture	2		
	Subcutaneous patch migration	2		
	Diaphragmatic stimulation	1		
	No therapy delivered	1		

Complications	Results	Number Events (E) (N=130)	Incidence Rate (%E/ Device Months)	Mean Time Between Events (Months)
Suspected lead problem		(10)	0.12	827
	Loss of capture	4		
	Undersensing	4		
	Oversensing (shock delivery)	1		
	Pocket stimulation	1		
Implant technique problems		(8)	0.10	1034
	Lead damage (over-stretched)	4		
	Communication difficulty (implanted upside down)	1		
	Lead damage (tip damaged)	1		
	Oversensing (implanted without capscrews)	1		
	Wrong patch implanted	1		
Unknown etiology		(7)	0.08	1182
	Oversensing	3		
	Loss of communication	2		
	Increased shock impedance	1		
	Undersensing	1		
Lead fracture: **Pacing-Epi (1)** **Endo (1)** **Commercial patches (2)** **Subcutaneous patch (1)**		(5)	0.06	1654
	Shock delivery	4		
	Observed during intervention (subcutaneous patch)	1		
Lead malposition		(5)	0.06	1654
	Loss of capture	2		
	High defibrillation thresholds	1		
	Pacemaker output sensing	1		
	Post-shock oversensing	1		
Oversensing **Connector problem (1)** **EMI (1)** **P-waves (1)**	Shock delivery	(3)	0.04	2757
RF ablation	Loss of communication (device damage)	(2)	0.02	4136
Communication noise	Premature ERI indicator	(1)	0.01	8272
Lead tubing torn during tunneling	Another lead implanted	(1)	0.01	8272

C. Potential Adverse Events

In addition to the adverse events reported in the clinical investigation, other adverse events may occur based on historical implant experience, including: cardiac tamponade, histotoxic reactions, perforation of the cardiac wall, pericarditis, phrenic nerve stimulation, pneumothorax, postoperative bleeding, septic shock, and slow or rapid pacing including "pacemaker runaway" (pacing at extremely high rates).

D. Adverse Psychological Events

Possible adverse psychological events associated with implantation of a defibrillator include: imagined shocking, fear of premature battery depletion, fear that shocking capability may be lost, fear of shocking while conscious, and dependency.

VIII. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative therapies for the treatment of life threatening ventricular arrhythmias, as deemed appropriate by the physician based upon electrophysiology testing and other diagnostic evaluation, include the use of antiarrhythmic medication, electrical ablation and cardiac surgery, electronic devices including pacemakers and other commercially available implantable defibrillators or a combination thereof.

IX. MARKETING HISTORY

As of May 8, 1995, there have been approximately 108 Res-Q™ ACD devices commercially distributed in foreign countries including: Austria, Israel, Belgium, Hong Kong, France, United Kingdom, Germany, The Netherlands, Canada and Australia. None have been withdrawn for any reason.

X. SUMMARY OF STUDIES

The qualification of the Res-Q™ ACD Epicardial Patch and NTL Systems included non-clinical laboratory testing such as components, leads and accessory, pulse generator and system (including software verification and validation), and biocompatibility tests. Several animal investigations were also conducted prior to initiation of the clinical studies.

A. Res-Q™ ACD Component Bench Tests

Analog and power microelectronic hybrids were subjected to operating life tests and wire bond pull strength tests. The batteries were subjected to a series of environmental stresses followed by visual inspection, dimensional analysis, x-ray, case temperature measurements, and electrical tests. Additionally, the Res-Q™ ACD batteries were evaluated under simulated use conditions by subjecting them to a low constant current drain (simulated pacing) and periodic high current pulses (simulating defibrillation). End of life and heat output characteristics were analyzed followed by destructive analysis. Finally, longevity testing was also performed to bound the battery life given best and worst case scenarios regarding number of shocks delivered and percent time paced. The Res-Q™ ACD high voltage capacitors were tested for performance under temperature extremes, constant voltage application, mechanical vibration, and life testing.

B. Res-Q™ ACD Device/System Bench Tests

- Electrical characterization testing of the Res-Q™ ACD was performed on electronic modules which were programmed to nominal settings and fixed gain. The characterization consisted of measurements of operating parameters versus supply voltage, temperature, and load. Further, pacing current measurements versus programmed pulse rate, pulse width and amplitude were also taken.

- Mechanical testing consisted of: mechanical shock bi-directional testing in three mutually perpendicular axes, vibration tests in the same three axes and temperature cycling. Tests were also performed to verify that the Res-Q™ ACD (models 101-01 and 101-01R) headers provide a leak-free fixation of the electrical connections between the Res-Q and its associated leads.

- Electromagnetic interference (EMI) testing was performed on the Res-Q™ ACD's *implant system* (device and leads) and the Res-Q™ ACD's *pre-implant system* (device, leads, test box, and patient cable). These systems, in various orientations, were exposed to radiated 450 MHz, 27.5 MHz and 2450 MHz circularly polarized pulsed electromagnetic fields. *Pre-implant systems* demonstrated susceptibility. As a result of this testing, labeling was added to the physician's manual on the possible effects of EMI during the implant procedure and how to minimize its effects. Testing was also performed to determine the effects of three different electronic article surveillance (store security) systems on the Res-Q™ ACD with the device oriented both parallel and perpendicular to the transmitter. As a result of this testing, labeling has been included in the physician's manual indicating that certain sources of electromagnetic interference may interfere with proper device operation (including inappropriate shocks).

- A storage temperature evaluation was conducted in which Res-Q™ ACDs were placed in a temperature chamber for two 48 hour periods, first at -5 degrees Centigrade and then at +55 degrees Centigrade, in order to verify the labeled storage temperature extremes. Final electrical testing after each cycle demonstrated that the Res-Q™ ACDs were unaffected by these extremes.

- Testing was performed on Res-Q™ ACDs to evaluate the effects of external defibrillation and electrosurgery equipment on the function of the Res-Q™ ACD. As a result of this testing, labeling has been included in the physician's manual to describe the possible effects of external defibrillation and electrocautery on the Res-Q™ ACD.

- The Res-Q™ ACD system software, consisting of the Res-Q™ ACD device software, the model 531-30 GRAPHICS program module, and the Rx2000™ GRAPHICS programmer, underwent a series of qualification tests. This testing was functional in nature and it verified that the software conformed with the product specifications and product labeling.

- For stock rotation purposes the maximum shelf life for the Res-Q™ ACD has been set at 11 months. This time period represents the amount of time allowed between capacitor reforms at room temperature and is equivalent to a 4-month reform schedule at body temperature.

- Packaging materials have been evaluated for bacteriological barrier properties and package seal integrity to assure sterility is maintained during the stated shelf life of the Res-Q™ ACD and its accessories.

C. Lead and Accessory Bench Tests

Testing of Intermedics epicardial patch leads included electrical and mechanical tests: cyclic axial fatigue flex testing, exposure to multiple high energy shocks, thermal shock, isolation resistance, and electrical continuity tests. Additional tests were also performed to verify the compatibility of the CPI A67 and L67 Epicardial Patch leads with the Res-Q™ ACD pulse generator. The Res-Q™ ACD accessories, patient cables, test box, and test load were all subjected to various mechanical and electrical qualification tests.

D. Biocompatibility Tests

Tissue/fluid contacting materials were evaluated for their biocompatibility: irritation tests, sensitization, cytotoxicity, acute toxicity, hemolysis, pyrogenicity, mutagenicity, implantation tests, and subchronic toxicity tests. Testing was not performed on the metallic materials which have a long history of use as implantable materials. Further, long term biocompatibility testing was not required on the soluble polyethylene glycol (PEG) which is used to encapsulate the fixating screw tip of Intermedics' transvenous lead because PEG is excreted from the body acutely.

E. Animal Studies

Compatibility of the commercially available CPI epicardial patches with the Res-Q™ ACD were conducted through an acute study consisting of seven animals and evaluated the following: bradycardia support, tachyarrhythmia detection and termination, and histological effects. Five animals were used in the chronic study to provide the long term data in evaluating biostability of the system. The results of the chronic testing led to a redesigning of the header to provide improved strain relief on the lead/adapter connector interface.

Acute lead only studies of an early design of the Intermedics Epicardial Patch lead were undertaken in 30 animals to study the electrical and mechanical performance of the leads. A chronic study using seven animals evaluated the chronic performance of the pulse generator/lead system. Various lead design changes such as header revisions, spot welding at the crimp sleeve, etc. resulted from these early studies. Subsequent to the design changes, a final chronic system animal study was instituted using six animals to assess the Res-Q™ ACD and the final model 497-01 epicardial patch design.

Several other acute lead-only studies and a chronic study evaluated the NTL system's electrical and mechanical characteristics as well as their histological effects: nine animals consisting of a model 497-05 right ventricular lead and a model 497-15 subcutaneous patch in the acute study and six animals in the chronic study and two acute studies consisted of the NTL lead system using a right ventricular lead model 497-06 (nine animals) and superior vena cava lead model 497-16 (six animals).

F. Clinical Studies

Clinical studies further evaluated the safety and effectiveness of the Res-Q™ ACD System. The two studies were initiated under separate IDEs with the patch series beginning approximately two years prior to initiation of the NTL study. The first study, initiated on August 10, 1990 under IDE #G900134, was conducted using CPI A67/L67 epicardial patch leads. The study was later amended to include the Intermedics epicardial patch leads. The second study was initiated on October 14, 1992 under IDE #G920047 and used Intermedics Non-thoracotomy (NTL) lead system. The information reported below reflects the data collected as of May 8, 1995 in the patient populations as of August 18, 1994. All participating centers used a common protocol.

1. Objectives

Like other commercially available systems, the Res-Q™ ACD system only attempts to terminate an episode of ventricular tachycardia (VT) or ventricular fibrillation (VF), and does not prevent their occurrence. The overall objective of the Res-Q™ clinical studies was to demonstrate the safety and effectiveness of the Res-Q™ Epicardial Patch and NTL systems in treating ventricular tachyarrhythmias in the indicated population. The following general objectives were outlined in the clinical protocols of each study:

- To demonstrate clinically acceptable: one-year cumulative survival probabilities relative to mortality endpoints for Res-Q™ ACD patients; incidence rate for device related observations and complications; and incidence rate relative to unanticipated adverse device related events.

- To determine whether the Res-Q™ ACD device in the epicardial patch and NTL lead system configurations can appropriately detect and terminate induced and spontaneous episodes of ventricular tachycardia and fibrillation.

2. Patient Population and Gender Bias Analysis

a. Res-Q™ ACD Patch Study (G900134) Patients

There were 178 patients who were implanted with the Res-Q™ ACD and epicardial patch leads (157 had CPI® epicardial patches and 21 had Intermedics epicardial patches) using thoracotomy lead implantation techniques. Twenty-seven centers participated in the multicenter study with 163 patients implanted for six months or more and 152 patients for twelve months or more at the May 8, 1995 data cutoff.

b. Res-Q™ ACD NTL Study (G920047) Patients

There were 235 patients who were implanted with the Res-Q™ ACD and NTL lead systems (177 used a RV lead and subcutaneous lead combination whereas 58 used a RV lead SVC lead combination). Twenty-six centers participated in the multicenter study with 214 patients implanted for six months or more and 182 patients implanted for twelve months or more at the May 8, 1995 data cutoff.

Table 3. Description of Res-Q™ ACD Patient Population (N = 178 patch and 235 NTL)

Characteristics	Res-Q™ ACD Patch Study		RES-Q™ NTL Study	
Mean age at implant years (Range)	63	(32-83)	63	(17-81)
Gender:				
Male	154	(87%)	195	(83%)
Female	24	(13%)	40	(17%)
Mean ejection fraction, % (Range)	34%	(10-70)	31%	(6-73)
NYHA (New York Heart Association)				
I	36	(20%)	54	(23%)
II	104	(59%)	132	(56%)
III	33	(19%)	47	(20%)
IV	4	(2%)	2	(1%)
Not Reported	1		0	
Primary Cardiac Disease:				
Coronary artery disease	139	(79%)	173	(74%)
Cardiomyopathy	22	(13%)	44	(19%)
Other	15	(8%)	17	(7%)
Not Required	2		1	
Primary Arrhythmia:				
VT	102	(58%) 45	145	(61%)
VT/VF		(25%)	53	(23%)
VF	30	(17%)	37	(16%)
Not Reported	1		0	
Most Common Defibrillating Lead System Configuration	CPI Large Patches		RV coil / Subcutaneous Patch	
Defibrillation Threshold (DFT) Mean ±SD (Range)	9.6 ± 6.4 Joules (1.8 - 27.2)		15.4 ± 6.2 Joules (1.9 - 38.1)	

Gender Bias Analysis: Of all patients enrolled, 15% (N=64/413) were females. Inclusion and exclusion criteria were chosen to avoid gender bias. The preponderance of male patients reflected both the gender referral pattern for cardiac disease and the severity of the disease in the centers involved. Analyses of safety and effectiveness relative to male and female patients indicated no differences between the genders. A chi square analysis did not show any significant associations between the gender and implant indications or occurrence of coronary disease. Logistic regression did not disclose any correlation of gender with either coronary artery disease or cardiomyopathy.

3. Study Design and Comparison Study Group

The Patch and NTL clinical trials were conducted as prospective, non-randomized trials using historical controls. When the Intermedics patches were made available, the protocol included randomization of patients to receive Intermedics or CPI® patches. This impacted only a small number of patients. The patch study enrollment tapered off with the availability of a nonthoracotomy lead system due to the less invasive nature of the surgical procedures. Without a prior Intermedics ICD (implantable cardioverter defibrillator) device to use as a comparison, the control populations were selected from published scientific literature including journal articles and publicly released Summaries of Safety and Effectiveness Data from other commercially available ICDs. Specifically, regarding the latter, the Res-Q™ Patch System was compared to the Medtronic® PCD® and Ventritex® Cadence®; the Res-Q™ NTL System was compared to the CPI/Guidant Endotak® Lead System and the Medtronic® Transvene® Lead System.

4. Clinical Experience & Results

Statistical Analysis: The safety and effectiveness of the Res-Q™ Patch and NTL Systems were proven through various statistical analyses. The statistical methods used in analyzing the stratified data were: F-test and Kruskal-Wallis tests to test the null hypothesis of no significant differences in location among factor levels of the major stratification variables • Stepwise Least-Squares Regression analysis to systematically identify baseline variables and patient characteristics • Chi-square Tests to test Homogeneity • Generalized Linear Models to analyze incidence rates of Complications and Observations • Longitudinal Regression applied to time dependent endpoints • Stepwise Logistic Regression applied to binary response and ordinal response variables • Cox Regression to analyze mortality endpoints • The Kaplan-Meier Product-Limit Survival method to analyze mortality endpoints • Weibull Regression to fit regression equations to mortality survival data which took into account the effects of significant concomitant variables • Confidence Intervals on the Poisson Rate Parameter λ calculated with the normal approximation formula.

a. Induced and Spontaneous Arrhythmia Episode Experience

One of the primary effectiveness endpoints was to demonstrate that these systems appropriately detect and terminate induced and spontaneous ventricular tachyarrhythmias. The data presented below for induced VT and VF episodes is from the predischarge and 4-month follow-up. The spontaneous events were tabulated from the Res-Q™ ACD's diagnostic counters (Tables 4 and 5 below).

Table 4. Arrhythmia Conversion: Patch Population (N = 178)

Arrhythmia Classification	Induced / Spontaneous	Number of Episodes	Arrhythmia Converted by Self	Arrhythmia Converted by Device
VT	Induced	291	7 (2%)	284 (98%)
	Spontaneous	3844	61 (2%)	3783 (98%)
VF	Induced	306	7 (2%)	299 (98%)
	Spontaneous	560	8 (1%)	552 (99%)

Table 5. Arrhythmia Conversion: NTL Population (N = 235)

Arrhythmia Classification	Induced / Spontaneous	Number of Episodes	Arrhythmia Converted by Self	Arrhythmia Converted by Device
VT	Induced	298	6 (2%)	292 (98%)
	Spontaneous	4081	54 (1%)	4027 (99%)
VF	Induced	513	9 (2%)	504 (98%)
	Spontaneous	604	5 (1%)	599 (99%)

b. Patient Survival

Patient survival data provided not only effectiveness information, but also served as the primary safety endpoint. The number of patient deaths was classified into various categories (Table 6.). One year actuarial survival analyses were also performed. The results were comparable to the historical controls.

Table 6. Patient Death and One Year Survival Results Res-Q™ ACD (N=25) Patch and (N=33) NTL

Death Classification	Res-Q™ ACD Patch Population		Res-Q™ ACD NTL Population	
	Number of Deaths	1 Yr. Survival Probability	Number of Deaths	1 Yr. Survival Probability
Total Mortality	25	91%	33	90%
All Cardiac Deaths				
Sudden Cardiac Deaths	4	98%	4	99%
Non-Sudden Cardiac Deaths	10	97%	24	92%
Non-Cardiac Deaths	9	96%	5	99%
Unknown	2	N/A	0	N/A

c. Clinical Events (Observations and Complications)

For purposes of the clinical study, the reported medical events were identified as observations and complications. An observation was defined as a symptomatic or asymptomatic clinical event with potential adverse effects, which does not require intervention, and can be corrected by reprogramming. A complication is a similar clinical event but which cannot be treated or resolved by reprogramming the device and requires intervention other than reprogramming. Intermedics reported no statistical difference between the Res-Q™ clinical studies' complication or observation rate and that presented in the historical controls. (Specific details regarding these events can be found in previous tables, see Tables 1 and 2.)

Unanticipated Adverse Device Effects. Four unanticipated adverse device effects (UADEs) were exhibited in the clinical studies. These events were related to (1) oversensing related to hardware anomaly, (2) short header design, (3) evoked T-wave undersensing ("therapy runout"), and (4) faulty electrolytic defibrillation capacitor. More than 50% (43/75) of the explants were due to the vendor-related faulty defibrillation capacitor. Design changes through hardware and software revisions have been incorporated into the device in order to prevent the observed unanticipated adverse device effects from occurring in the future.

XI. DEVICE ACCOUNTABILITY, RELIABILITY, AND LONGEVITY

Table 7 below provides a summary of all Res-Q™ ACD pulse generators and leads used in the Res-Q™ ACD clinical investigations.

Table 7. Device Accountability
Total devices implanted: Patch (N = 211 devices) and NTL (N=255 devices)

	Res-Q™ ACD Patch	Res-Q™ ACD NTL
Devices Implanted:	(211)	(255)
Still Active	134	196
Out-of-Service	75	58
Changed Lead System	2*	1**
Out-of Service Devices:	75	58
Due to Deaths	(25)	(33)
Not Returned	6	16
Analyzed	19	17
Due to Explantation	(50)	(25)
Unanticipated Adverse Events	32	11
Complications	13	13
Normal End of Service/Elective	3	0
Heart Transplantation	2	1
Returned Devices	69	40
Analysis Results:		
-Tested Within Engineering Specifications	26	21
-Faulty Defib. Capacitor	31	14
-Normal End of Service	3	0
-Adapter Fracture due to original header design	3	0
-Short Circuit -improperly insulated setscrew	1	0
-Component Failure - battery capacitor	2	2
-Undetermined failure after VT ablation	1	0
-Device damaged during analysis	1	0
-Battery depletion consistent with use	0	2
-Analysis in process	0	1
-Excessive current drain due to battery capacitor	1	0

* Two Patch patients changed to NTL study (the Res-Q™ devices were not explanted) after the patient population cutoff date of 8/18/94.
** One NTL patient changed to the Patch study (the Res-Q™ device was not explanted) prior to 8/18/94.

XII. CONCLUSIONS DRAWN FROM STUDIES

Prior to initiation of the clinical studies, the Res-Q™ ACD Epicardial Patch and NTL Systems have been subjected to rigorous in-vitro testing at the component, device, and system levels. The tissue and fluid contacting materials were evaluated for their biocompatibility. Extensive animal studies were also conducted in which various design changes was implemented resulting from the early studies. The results of in-vitro and in-vivo studies provide reasonable assurance that the Res-Q™ ACD Epicardial Patch and NTL Systems are safe and effective when used as indicated in the labeling.

XIII. FDA DECISION

On August 21, 1995, the results of the Res-Q™ ACD Epicardial Patch and NTL Systems clinical investigations were presented to the Circulatory System Devices Panel which recommended approval with conditions. The recommendation was based on the following conditions: (1) incorporate minor labeling changes to the instructions in the Physician's Manual related to patient follow-up, (2) agree to devise a detailed protocol to conduct a post-approval study specific to patients implanted with Intermedics epicardial patches (due to the small number of implanted systems using these leads), (3) include a requirement to provide minimal physician training which may be conducted on-site prior to implantation of this device, (4) revise the second indication for use in the labeling to read, "recurrent, poorly tolerated sustained ventricular tachycardia," and (5) clarify the labeling concerning telephone monitoring. FDA concurred with the recommendations of the panel.

On September 12 and November 13, 1995, Intermedics submitted amendments to the application providing the information recommended by the panel and required by FDA. FDA approval is subject to the applicant's compliance with the "Conditions of Approval for Implantable Defibrillators and Programmers" (Attachment A), and the conditions that the sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specify the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

On October 25, 1995, FDA completed an inspection of Intermedics' manufacturing facility (Angleton, TX) and determined that the manufacturer was in compliance with the Device Good Manufacturing Practices Regulation (21 CFR part 820).

XIV. APPROVAL SPECIFICATIONS

Intermedics will conduct a post-market surveillance study of the Res-Q™ ACD Epicardial Patch and NTL systems as required by the 1990 Safe Medical Device Act. In addition, the post-approval reports shall include the following information and submit appropriately either as a separate supplement or an annual report: (1) post-approval study on the remaining 16 patients currently implanted with the Intermedics Model 497 series patch leads, (2) follow-up on the remaining few patients implanted with a "faulty" capacitor, (3) test reports of further EMC (electromagnetic compatibility) testing from new sources of electromagnetic radiation, (4) updated life-testing information conducted on the pulse generator's power source (batteries), high energy defibrillation capacitors and leads, (5) upgraded calculations of device longevity based on accumulating clinical experience, (6) software revisions to correct remaining minor software anomalies, and (7) revisions to the patient manual.